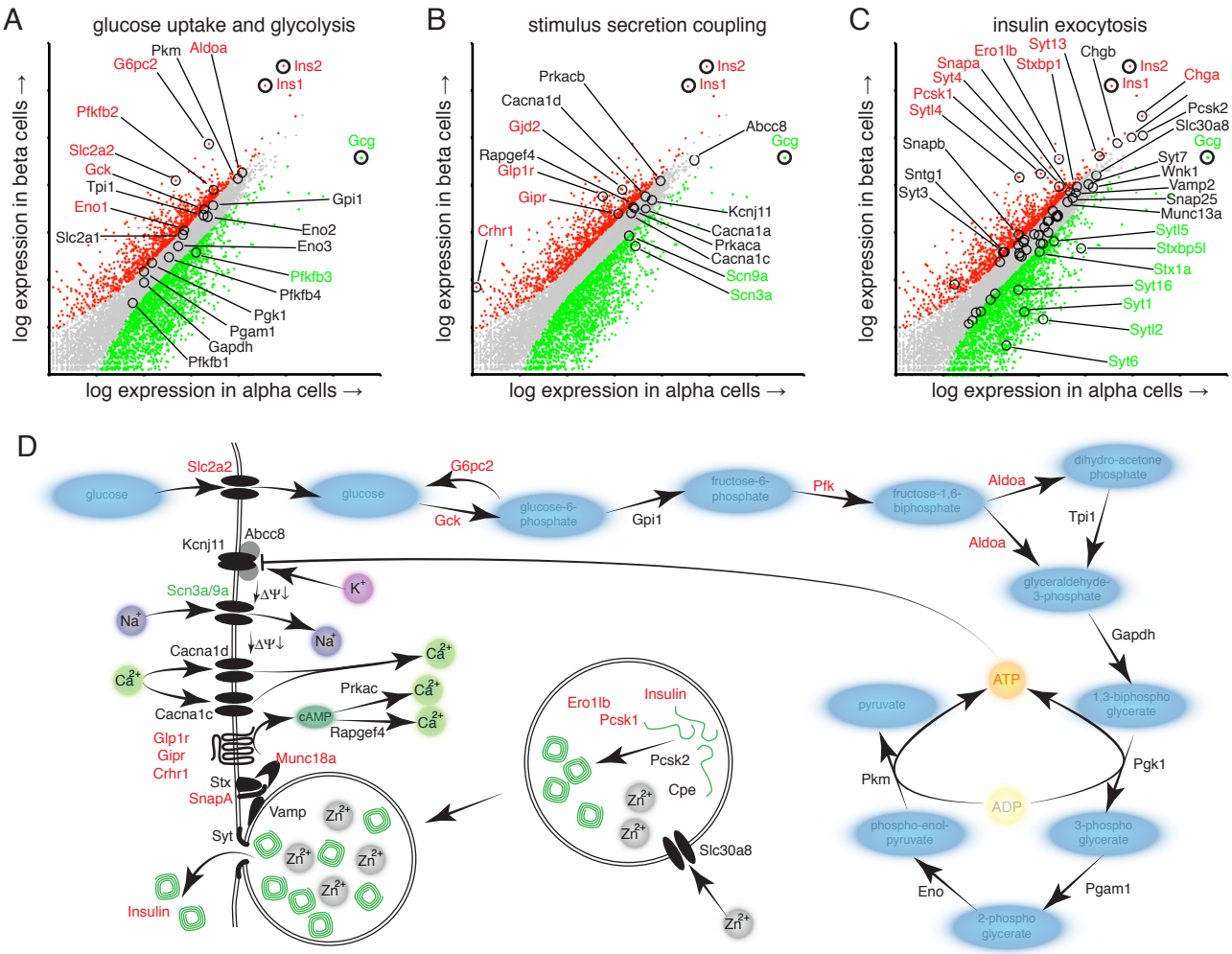

Additional data file 6: Stimulus-appropriate secretion of insulin constitutes the core function of the beta cell. We therefore looked at the genes required for glucose uptake and glycolysis (A), stimulus secretion coupling (B) and insulin exocytosis (C) - interconnected processes vital for the release of insulin dependent on ambient glucose concentration as summarized schematically in (D) and reviewed in detail elsewhere [1-3]. Among the most significantly enriched genes in our data that are involved in beta cell stimulus secretion coupling are the facilitated glucose transporter Slc2a2 (a.k.a. Glut2) and glucose-6-phosphate convertase 2 (G6pc2), which are selectively expressed in mouse beta cells [4, 5]. G6pc2, which regulates fasting glucose [6-8] and is an autoantigen for type 1 diabetes [9], is the 11th most abundantly expressed gene in mouse beta cells (Figure 3C). Ero 1-like beta (Ero1lb), involved in disulphide formation between the insulin amino acid chains, and proprotein convertase subtilisin/kexin type 1 (Pcsk1), specifically required for insulin but not glucagon processing, are highly enriched in beta cells as expected (Figure 3D). The most significantly enriched in mouse beta cells among the many proteins that coordinate docking and fusion of the secretory vesicle with the cell membrane is synaptotagmin-like 4 (Sytl4, a.k.a. granuphilin) (Figure 3E), which in mouse islets is required for granule docking to the plasma membrane while preventing vesicle fusion and insulin release [10, 11]. Finally, class B GPCRs such Glp1r, Gipr and Crhr1 that can potentiate glucose-stimulated insulin secretion [12, 13], are significantly enriched in beta cells.

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